

REMARKS

Claims 1-3, 6-20, 23, 26-29 and 32-45 were pending in this application. Claims 1, 15, 17, 18 and 27 were amended. Thus claims 1-3, 6, 10-20, 23, 26-29 and 32 are still pending in the present application and under consideration. Applicant maintains that the amendments do not introduce any new matter. The claim amendments are the same amendments submitted in the April 28, 2006 Amendment but which were not entered according to the June 1, 2006 Office Action for reasons of record.

Declaration

Applicants thank the Examiner for removing the objection to the Declaration.

Objection to the Amended Disclosure under 35 USC 132(a)

The amendments filed 11/7/05 to Table 2 were objected to by the Examiner under 35 USC 132(a) for introducing new matter. The Examiner has previously pointed out a discrepancy in Table 2, i.e., reciting the same number in two columns of the Table.

In response, Applicants maintain that the presence of the same number in two columns of Table 2 is indicative of a typographical error. Based on the Examiner's remarks, Applicant went back to the NIH grant that was filed concurrently with the instant patent application and was based on the same data. Applicant corrected Table 2 of the instant specification, using numbers provided in the NIH grant application (page 15). Thus, the proper column labels for Table 2 should be 10 µg/mL and 100 µg/mL, consistent with the data in the grant proposal.

As stated in the MPEP:

An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction. *In re Oda*, 443 F.2d 1200, 170 USPQ 268 (CCPA 1971).

[MPEP 2163.07]

Applicants urge that the typos in Table 2, constitute an obvious error: while specification in the paragraph immediately preceding Table 2 refers to “concentrations” in plural, Table 2 provides identical concentration value in both columns. The data presented in the left column differ from the data in the right column, although columns are identically labeled.

The entry of the corrections from the NIH grant that was filed based on the same data should be allowed because one skilled in the art would not only recognize the existence of error in the specification, would appreciate the proper ranges of concentrations from Table 3 (providing 12 ug/mL and 111ug/ml in lines 3 and 5) and from the specification, page 37, line 16, providing concentrations of 10ug/mL and 0.12 ug/mL, and because the typo does not relates to the claimed subject matter and the correction does not affect the scope or enablement of the currently pending claims.

Favorable reconsideration is earnestly solicited.

Rejection under 35 U.S.C. 112, Second Paragraph

Applicants than the Examiner for removing the rejection under 35 U.S.C., second paragraph.

Rejection under 35 U.S.C. 112, First Paragraph

The Examiner claims 1-3, 6, 10-20, 23, 26-29 and 32 are rejected under 35 USC 112, first paragraph, enablement requirement. The Examiner’s alleges that the specification does not enable one of ordinary skill in the art to make catalytic antibodies that can attach a label to a molecule (1) due to

the lack of working examples and (2) because, in Examiner's opinion, the art of catalytic antibodies, unlike the art of monoclonal antibodies, is unpredictable.

Applicant respectfully traverses. First, working examples are not required to satisfy the enablement requirement (MPEP Section 2164.02). As admitted by the Examiner, the Specification provides extensive disclosure of the methods of making and using catalytic antibodies, as well as target molecules to be modified by disclosed antibodies. Every stage of the process is disclosed in a great detail therefore enabling a person of ordinary skill in the art to practice the claimed invention without undue experimentation. The disclosure also teaches how to test the antibodies for the desired activity, e.g., catalytic antibody can be identified by screening human phage antibody display libraries against an antibiotic-target conjugate. The specification teaches selecting labels that exhibit a low but detectable reaction with the desired target in the absence of a catalyst, for example, the conjugation reaction of β -lactam antibiotics with proteins (Specification, page 9, line 15 – page 10, line 10). The same passage in the specification also notes that the fact that the uncatalyzed reaction can occur at a slow rate places a lower burden on the catalyst and may only require that the catalyst bind to both the target and label so as to hold them in close proximity and increase their effective concentrations. In addition, the specification is not limited to selection of catalytic antibodies by panning phages and also teaches a variety of other approaches including directed evolution under selective pressure and/or the mutation of catalysts with similar chemical activities but different structural specificity. The fact that the specification does not provide working examples of the elicitation of catalytic antibodies does not support the Examiner's rejection.

The Examiner fails to explain why the methodology taught in the specification would not enable one of ordinary skill in the art to practice the claimed invention. As such, the Examiner's arguments are without merit and the pending claims should be found enabled in satisfaction of 35

U.S.C. § 112, ¶ 1. *E.g., Marzocchi*, 439 F.2d at 224, 169 U.S.P.Q. at 369-70; *Pishevar*, 2002 WL 1801082, at *4-*5; *Dow*, 1997 WL 33116047, at *2.

Applicants submit that one of ordinary skill in the art would be able to practice the presently claimed subject matter in view of the specification and the prior art without undue experimentation. The test for enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 190 U.S.P.Q. 214 (CCPA 1976). See also, MPEP § 2164.01. The fact that experimentation may be complex does not necessarily make it undue if those skilled in the art typically engage in such experimentation. *In re Certain Limited - Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983); *M.I.T. v. A.B. Fortia*, 227 U.S.P.Q. 428 (Fed. Cir. 1985); *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). See also, MPEP § 2164.01.

Contrary to the Examiner's suggestion, the specification need not provide examples or specific description of embodiments for the entire scope of the invention. Detailed procedures for making and using an invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention [MPEP §2164]. A patent does not teach, **and preferably omits**, what is well known in the art. *In re Buchner*, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 221 U.S.P.Q. 481, 489 (Fed. Cir. 1984). [See also, MPEP § 2164.01].

Second, the Examiner's reliance on Janda et al., Schultz, Sinha and Yu to support the allegation of unpredictability is misplaced. While citing Janda et al., Schultz, Sinha and Yu the Examiner also implicitly admits that at least one catalytic antibody was obtained in each of the cited references, showing that appropriate antibody activity is achieved despite any inherent variability associated with generating catalytic antibodies (or antibodies in general). The Examiner, describes the experimental effect

observed in Janda et al., but fails to mention that Janda et al. explain the effect and further teaches that “From this findings an approach is suggested to improve antibody catalytic efficiency.” (Janda et al, page 2504). Yu et al and Schultz (two studies coming from the same research group) teaches that “Both this study and recent work by Reymond et al. show that haptens containing a positive charge corresponding to the anomeric center of a cyclic acetal can elicit antibodies with hydrolytic activity.” (Yu et al., page 340, right-hand column). Finally, although Taffik et al. suggests that the rates achieved to date were “modest,” Taffik et al. does review a large number of examples of successful generation of catalytic antibodies.

Applicants urge that the state of the relevant art is high. The following two publications reflect the high state of the relevant art. Copies of the references are enclosed for the Examiner’s convenience as supporting reference material.

(1) Nevinsky GA, Semenov DV, Buneva VN.

Catalytic antibodies (Abzymes) Induced by Stable Transition-State Analogs

Biochemistry (Moscow) 2000; 65(11): 1233-44.

The Nevinsky reference includes twenty-four examples compiled in a comprehensive table format of successful catalytic antibodies productions where transition-state analogs were employed. This review further demonstrates that in view of the high state of relevant art, the applicants had possession of the instant invention.

(2) Stevenson JD and Tomas NR.

Catalytic antibodies and other biomimetic catalysts

Nat. Prod. Rep. 2000; 17: 535-577.

The Stevenson reference is a comprehensive review which provides multiple examples of the successful use of various transition state analogs in eliciting catalytic antibodies for both ester and amide hydrolysis (chapters 2.6 and 2.7).

Applicant urges that the claims are fully enabled by the disclosure in the Specification and further in view of the high state of relevant art. Although the specification discloses an embodiment in which a β -lactam antibiotic is attached to a target molecule, the teachings of the specification are considerably broader. The section of the specification describing “labels” for modifying target molecules (Specification, page 8, line 22 – page, line 10) lists a variety of suitable labels for use with the methods of the invention and also describes properties of the labels that can be used to select for other suitable labels.

The Examiner specifically alleges that the Specification is not enabling with respect to non-naturally occurring enzyme (Claims 17-20, 23 and 26).

Applicants respectfully traverse. The specification clearly discloses the applicability of all methods to “Catalysts of biological origin such as enzymes. . .” (Specification, page 7, line 25). The specification goes further to note that “Catalytic antibodies are especially preferred catalysts.” (Specification, page 8, line 3). Every method disclosed in the specification in great detail is applicable to naturally occurring enzymes that are modified as disclosed in the specification (thus, resulting in non-naturally occurring enzymes). Even further, while the Examiner alleges that the art of catalytic antibodies is unpredictable, the Examiner makes no such argument in relation the field of enzyme modification. A number of companies successfully practice in this area of technology, the list including, but not limited to, Direvo AG (<http://www.direvo.com/>), Diversa Corp. (<http://www.diversa.com/>) and Maxygen (<http://www.maxygen.com/nopage.php>).

The Examiner fails to explain why the methodology taught in the specification would not enable one of ordinary skill in the art to practice the claimed invention. As such, the Examiner’s arguments are without merit and the pending claims should be found enabled in satisfaction of 35

U.S.C. § 112, ¶ 1. *E.g.*, *Marzocchi*, 439 F.2d at 224, 169 U.S.P.Q. at 369-70; *Pishevar*, 2002 WL 1801082, at *4-*5; *Dow*, 1997 WL 33116047, at *2.

Thus, one of ordinary skill in the art would readily recognize from the original disclosure that the present invention is enabled. Therefore, Applicant requests that this rejection be withdrawn.

Claims 1-3, 6, 10-20, 23, 26-29 and 32 were rejected under 35 USC 112, first paragraph, written description requirement. (Office Action, pages 6-7).

In response, Applicant respectfully traverses. Applicant submits that the function of the written description requirement is to ensure that a patent is granted to inventors who had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by them; how the specification accomplishes this is not material. *In re Smith*, 178 U.S.P.Q. 620 (CCPA 1973).

Therefore, the test for written description under 35 U.S.C. §112, first paragraph, is whether the originally filed specification reasonably conveys to a person having ordinary skill that Applicants had possession of the subject matter later claimed. *In re Kaslow*, 217 U.S.P.Q. 1089 (Fed. Cir. 1983). [See also, MPEP, Section 2163.02].

The Specification provides extensive disclosure of the methods of making and using catalytic antibodies, as well as target molecules to be modified by disclosed antibodies. Every stage of the process is disclosed in a great detail therefore enabling a person of ordinary skill in the art to practice the claimed invention without undue experimentation. The disclosure also teaches how to test the antibodies for the desired activity, e.g., catalytic antibody can be identified by screening human phage antibody display libraries against an antibiotic-target conjugate. The specification teaches selecting labels that exhibit a low but detectable reaction with the desired target in the absence of a catalyst, for example, the conjugation reaction of β -lactam antibiotics with proteins (Specification, page 9, line 15 – page 10, line 10). The same passage in the specification also notes that the fact that the uncatalyzed

reaction can occur at a slow rate places a lower burden on the catalyst and may only require that the catalyst bind to both the target and label so as to hold them in close proximity and increase their effective concentrations. In addition, the specification is not limited to selection of catalytic antibodies by panning phages and also teaches a variety of other approaches including directed evolution under selective pressure and/or the mutation of catalysts with similar chemical activities but different structural specificity. The Specification also makes it clear that the disclosure applies to non-naturally occurring enzymes. (Specification, page 7, line 25)


Thus, one of ordinary skill in the art would readily recognize from the original disclosure that Applicants invented the presently claimed subject matter. Applicants submit that the Examiner's allegation that the specification is deficient in that it does not show working is not relevant to a determination of whether Appellants' have satisfied the written description requirement of the first paragraph of 35 USC 112. Therefore, Appellants request that this rejection be reversed.

In view of the foregoing, it is respectfully submitted that this application is now in condition to be allowed and the early issuance of a Notice of Allowance is respectfully solicited. If there are any issues or amendments the Examiner wishes to discuss, the Examiner is encouraged to contact the undersigned.

Respectfully submitted,
Kramer Levin Naftalis & Frankel LLP
Attorneys for Applicant

Dated: July 28, 2006

By:



Barry Evans, Esq.
Reg. No. 22,802
Charles C. Achkar, Esq.
Reg. No. 43,311
1177 Avenue of the Americas
New York, New York 10036
Tel.: (212) 715-9100
Fax.: (212) 715-8000